REMARKS

In responding to the Office Action, Applicants conducted a telephone interview with Examiners Whaley and Moran on June 1, 2006. During this interview, the pending rejections raised by the Examiner were discussed. Applicants discussed amending claim 51 to include the elements of claim 1, which would clarify the pending 35 U.S.C. §112 rejections and possibly avoid the prior art rejections. Applicants also discussed that in various embodiments, the 5' tag of the amplification primer is design to contain, among other things, a copy of the sequence of nucleotides surrounding and including the polymorphic site of the target. After amplification of the target nucleic acid using primers comprising these special 5' tags, the resulting amplicons contain a mirror image of the polymorphic site (Mirror SNP) and the actual polymorphic site (Real SNP). See Figures 3 and 4. Using these tags in the amplification step allows for accurate and reliable identification of polymorphisms, particularly, in heterozygous and/or complex genotypes.

By this amendment, Applicants have amended the claims consistent with the interview. Claim 51 further defines the 5' tags and the amplification and identification steps consistent with the language of claim 1, which the Examiners indicated that they would consider. Support for claim 51 can be found, for example, in claims 1-3, and 15, Figures 3 and 4 and pages 50-51. Claim 52 has been amended to include that the 5' tag comprises the same nucleotide base as the wild-type nucleotide base or the mutant nucleotide base of the target and the tags are employed at a known ratio. New claim 62 and 63 include that the 5' tags differ by one nucleotide or just by the variant nucleotide. Support for claims 52, 62 and 63 can be found in the specification, for example, at page 11, line 20 to page 12, line 20, page 22, lines 11 to page 23, line 25, page 25, lines 17-34, page 36, line 21, to page 37, line 14, pages 50-51, page 68 and Figures 3-5.

Support for the new claims 64-68 can be found in the claims as originally filed. See, for example, the table below.

Claim	Support
64	Claim 10
65	Claim 46
66	Claim 16
67	Claim 17
68	Claim 18

No new matter has been added by this amendment. Applicants respectfully request entry of the amendments and allowance of the case.

Claim Objections

The Examiner objected to claims 51 and 52 for minor typographical errors. Applicants have amended the claims to remove the minor typographical errors. Accordingly, the objection is moot.

Rejection under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 51 and 52 as allegedly indefinite for certain alleged indefinite phrases in the preamble and body of the claims.

Applicants respectfully disagree with the Examiner and submit that the claims are definite to a person of ordinary skill in the art upon reading the specification. However, in order to expedite prosecution of the application, Applicants have amended the claims to remove the alleged indefinite terms as discussed during the interview. Applicants submit that the claims are definite to one of ordinary skill in the art and request reconsideration and withdrawal of the rejections based on 35 U.S.C. § 112, second paragraph.

Rejection Under 35 U.S.C. § 102(b)

The Examiner rejected claims 51 and 52 under 35 U.S.C. §102(b) as allegedly being anticipated by Pastinen et al. Clinical Chemistry (1996) 42:9, 1391-1397 (Pastinen). Applicants respectfully traverse this rejection.

For a rejection to be sustained under 35 U.S.C. §102(b), each and every element of the claims must be disclosed in the cited prior art reference. The Examiner alleges that Table 1 and p. 1392 of Pastinen anticipates the claims. Applicants respectfully disagree with the Examiner.

The claims have been amended to include that the amplification primer includes a 5' tag comprising a copy of the polymorphic site and at least one nucleotide surrounding the polymorphic site. Applicants refer the Examiner to Figure 3-5 of the specification, for example, where the 5' tag of the amplification primer is design to contain, among other things, a copy of the sequence of nucleotides surrounding and including the polymorphic site (e.g., A or G) of the target. After amplification of the target with these special 5' tags, the resulting amplicons contain a mirror image of the polymorphic site (Mirror SNP) and the actual polymorphic site (Real SNP). See, for example, Figure 4. Utilizing these 5' tags allows for accurate and reliable identification of polymorphisms, particularly, in heterozygous and/or complex genotypes. Applicants submit that Pastinen is silent on using 5' tags comprising a copy of the polymorphic site --the same nucleotide bases in sequence as the variant nucleotide (polymorphic site) flanked by the invariant nucleotide (the nucleotide that does not contain the polymorphic site) of the target nucleic acid.

In fact, Pastinen teaches that the 5' tags (tails) are random and should be used on the mini-sequencing detection primers.

> To make each of the detection primers different in length, **a random nucleotide tail was added to the 5' ends** of some of the primers as shown in Table 1. (Pastinen p. 1392, col. 1, emphasis added).

Applicants respectfully submit that Pastinen does not disclose, teach or suggest 5' tags comprising nucleic acids that mirror the polymorphic site and the nucleotides flanking the polymorphic site. Accordingly, Pastinen does not disclose each and every element of the claims and Applicants request that this rejection under 35 U.S.C. §102(b) be reconsidered and withdrawn.

Rejections Under 35 U.S.C. § 103(a)

The Examiner rejected claims 51 and 52 as allegedly obvious over US 2004/0038256 (Van Ness) in view of Pastinen. Applicants respectfully disagree with the Examiner, and traverse this rejection.

To establish a *prima facie* case of obviousness, all of the claim elements must be taught or suggested by the prior art. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Applicants refer the Examiner to the arguments made above regarding the Pastinen reference and submit that Pastinen does not disclose, teach or suggest 5' tags comprising nucleic acids that mirror the polymorphic site.

Van Ness does not rectify this defect. Van Ness does not disclose, teach or suggest 5' tags comprising nucleic acids that mirror the polymorphic site. Rather, Van Ness discloses oligonucleotide primers that contain an interrupted restriction endonucleases recognition sequence (IRERS) incorporated into the primer (Van Ness at paragraph 120 and Figures 1A –B and Figure 3).

After amplification of the target, Van Ness teaches digesting the amplicon with a restriction enzyme that recognizes the restriction site. After digestion, the nucleotide of interest (in a fragment that contains a 5'overhang) is subsequently detected by fluoresce polarization. Thus, Van Ness does not disclose, teach or suggest, using identification primers placed near the site of interest that are extended by one or more chain terminators using a polymerase to determine the identity of the variant nucleotide (polymorphism). Rather, Van Ness teaches using a restriction enzyme immediately after amplification to identify the nucleotide of interest.

In summary, Pastinen and Van Ness, alone or in combination do not disclose,

teach or suggest 5' tags comprising nucleic acids that mirror the polymorphic site, nor do they disclose, teach or suggest using a step of extending identification primers with chain terminators to identify the variant nucleotide (after the 5' tags are incorporated into the amplicon). Accordingly, the claims cannot be considered obvious and Applicants request that the rejection under 35 U.S.C. §103(a) be reconsidered and withdrawn.

Double Patenting Rejection

The Examiner provisionally rejected claims 51 and 52 for 35 U.S.C. §101 double patenting in view of claims 47 and 48 of co-pending U.S. Application No. 10/328,150 ('150 application). The claims have been amended so this provisional rejection is moot. However, Applicants will cancel the appropriate claims in '150 application once allowable subject matter is indicated.

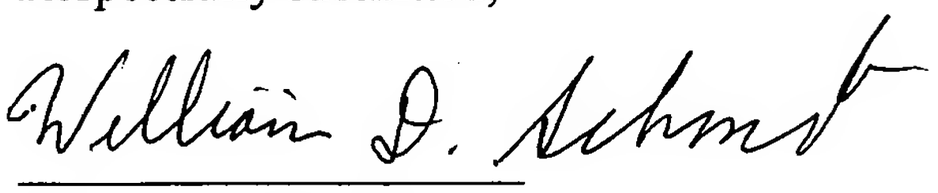
Conclusion

Reconsideration and allowance are respectfully solicited.

Enclosed is the fee for 1-month extension of time. No additional fee is believed to be due with respect to the filing of this amendment. If any additional fees are due, or an overpayment has been made, please charge, or credit, our Deposit Account No. 11-0171 for such sum.

If the Examiner has any questions regarding the present application, the Examiner is cordially invited to contact Applicant's attorney at the telephone number provided below.

Respectfully submitted,



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